Transport of peritoneal membrane assessed before and after the start of peritoneal dialysis

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Abstract

Background. Patients on peritoneal dialysis (PD) with high small solute peritoneal membrane transport have an increased risk of morbidity and mortality. The membrane transport is currently assessed by peritoneal equilibration test (PET), usually performed after the first month of PD because of the early increase of membrane transport after the start of PD. The aim of this study was the assessment of small solute peritoneal membrane transport before and after the start of PD.

Methods. The small solute peritoneal membrane transport was evaluated in 34 patients before the start of PD. Twenty-two patients were treated with continuous ambulatory peritoneal dialysis (CAPD) and 12 with automated peritoneal dialysis (APD).

Results. Four months after the start of PD, the small solute peritoneal membrane transport increased only in CAPD patients (D/PCreat, the ratio between dialysate solute concentration at the end of the PET and creatinine plasma concentration, changed from 0.66 ± 0.12 to 0.73 ± 0.07 in CAPD patients and from 0.64 ± 0.12 to 0.61 ± 0.07 in APD patients), and after about 16 months of PD, the peritoneal membrane transport was higher in CAPD patients (D/PCreat = 0.74 ± 0.06) than in APD patients (D/PCreat = 0.63 ± 0.10).

Conclusions. Performing the PET before and after the start of PD could provide relevant information about the characteristics of small solute peritoneal membrane transport and could be useful to evaluate the influence of PD modality on the changes in peritoneal membrane transport.

Keywords: automated peritoneal dialysis (APD); continuous ambulatory peritoneal dialysis (CAPD); peritoneal equilibration test (PET); peritoneal membrane transport

Introduction

Peritoneal transport characteristics play an important role in determining morbidity, mortality and management of peritoneal dialysis (PD) patients. Small solute peritoneal membrane transport is assessed by the peritoneal equilibration test (PET) [1]. Membrane peritoneal transport varies between patients and can change over time in the same patient [2–9].

Patients with high small solute membrane peritoneal transport have an increased risk of morbidity and mortality, in spite of their more rapid diffusive clearance of urea and creatinine [10–12]. However, in patients with high small solute membrane peritoneal transport, the increased risk of mortality could be mitigated by the optimization of the short dwell lengths using automated peritoneal dialysis (APD), combined with icodextrin, rather than continuous ambulatory peritoneal dialysis (CAPD) [12].

Ascertaining patients’ peritoneal membrane transport status early on during the PD training would, therefore, be highly advantageous to determine their optimal PD prescription at the start of PD therapy. However, a retrospective study [13] and a prospective study [14] showed that peritoneal membrane transport increased during the first weeks of PD therapy. Based on these studies, current clinical guidelines [15–17] recommend caution against performing PETs in the first month of PD commencement.

At the moment, there are no studies about the changes of peritoneal membrane transport before and after the start of PD. Furthermore, there are no studies about the influence of PD prescription at the start of PD on the peritoneal membrane transport.
The aim of this prospective study was the assessment of peritoneal membrane transport before the start of PD and then about 4 months (early) and about 16 months (late) after the start of PD (CAPD or APD) therapy.

Patients and methods

All incident patients starting PD at the A. Manzoni Hospital, Lecco, Italy, were studied from March 2004 to April 2007, after having given their informed consent.

During the break-in period (i.e., the time between the peritoneal catheter insertion and the start of PD), all patients underwent weekly peritoneal fast washing with a 0.5 l PD solution with a glucose concentration of 1.36% and lactate as a buffer; the washing was repeated three or four times and the peritoneal cavity was completely drained at the end of the procedure.

On the starting day of PD, all patients underwent the first PET. The PD modality was not randomized and based on patients’ preference or on medical need. The changes of PD modality were not allowed during the study. A 3.86% PET was performed in all patients on the morning of the first PD day and then 4 months and 16 months after the PD start. The dwell before each PET (overnight dwell, from 11.00 p.m. to 7 a.m.) was performed using a 2 l PD solution containing a glucose concentration of 1.36%, with lactate as a buffer, in all patients. The overnight dwell was performed also before the first PET in order to make the methods uniform. All patients were treated with lactate-buffered, conventional dialysis solutions. At the time of the tests, all patients had been peritonitis-free for at least 4 weeks. Blood samples were drawn at the start of the 3.86% PET, and fresh PD fluid (Dt0) samples were taken from the bag at the end of the infusion. After the complete infusion of a 2 l 3.86% glucose PD solution, 20 ml dialysate samples were taken at 60 and 240 min (D60′ and D240′) after flushing back 30 ml of dialysate. The patients were instructed to sit up or move about in bed before the drawing of each dialysate sample; otherwise, they remained recumbent during the test. After 240 min, the dialysate was collected by gravity for at least 20 min. The volume of the infused fresh PD solution and the drained dialysate was measured by weighing the bag and then subtracting the weight of the empty bag; no corrections were made for differences in the specific weight of the solutions.

Analytical methods

Plasma and dialysate creatinine, total protein and glucose concentrations were analysed using a Hitachi 717 (Hitachi Ltd, Tokyo, Japan); dialysate creatinine concentration was assessed by an enzymatic method in order to eliminate the effect of the high glucose dialysate concentration. The total dialysate sodium concentration was analysed twice using an IL 943 flame photometer (Instrumentation Laboratory, Milan, Italy).

Calculations

D/D0 was calculated as the ratio of dialysate glucose concentration between the end and the start of the PET. D/Pcreat was calculated as the dialysate solute concentration at the end of the PET divided by creatinine plasma concentration. Plasma water concentrations were used to calculate D/PNa60′ [18]. D/PNa60′ was calculated as the dialysate solute concentration at 60 min of the PET divided by sodium plasma concentration.

The glomerular filtration rate (GFR) was calculated as the average of the urea and creatinine clearances adjusted to body surface area.

Statistical analysis

Results were expressed as mean values ±1 standard deviation (SD) or ±1 standard error (SE) for normally distributed data. Median values and inter-quartile range were given for asymmetrically distributed data. Mean values ±1 SD of D/Pcreat was used to categorize PD patients, as reported elsewhere [9]. The patients were divided into cohorts according to the minimal number of PETs performed, so that changes in the transport characteristics of the peritoneal membrane were analysed in the same patients. Repeated measures analysis of variance was used to evaluate differences of the same variable between the first and the following PETs within each cohort [19]. The paired t-test and the Wilcoxon signed-rank test were used to evaluate differences of the same variable between the PETs for data with normal and asymmetrical distribution, respectively.

<table>
<thead>
<tr>
<th>Table 1. Peritoneal membrane characteristics in all PD patients</th>
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<tbody>
<tr>
<td>1st PET</td>
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<tr>
<td>UF (ml)</td>
</tr>
<tr>
<td>D/D0</td>
</tr>
<tr>
<td>D/Pcreat</td>
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<tr>
<td>D/PNa60′</td>
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<td>No. of patients</td>
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PET, peritoneal equilibration test.

Multiple analysis of variance (MANOVA) was used to compare changes over time of the studied parameters between patients treated with CAPD and APD and the influence of peritonitis on the same parameters. A P-value ≤ 0.05 was considered as significant. All statistical analyses were performed using JMP (SAS Institute Inc., Cary, NC, USA) for the Windows statistical software (release 4.0).

Results

A total of 34 patients (M/F: 18/16) began PD treatment during the study period. PD was started 1.4 (1.2–1.6) months after the insertion of the peritoneal catheter. Primary diagnoses of chronic kidney disease were glomerulonephritis in 10 (29.4%) patients, hypertensive nephropathy in 3 (8.8%) patients, adult polycystic renal disease in 2 (5.9%) patients, reflux nephropathy/interstitial nephritis in 2 (5.9%) patients, diabetic nephropathy in 12 (35.3%) patients and small kidneys/unknown in 5 (14.7%) patients. At the start of PD, patients had a mean age of 63 ± 12 years. Twenty-two patients were treated with CAPD and 12 with APD. At the start of PD, four exchanges of 2 l with a 1.36% glucose PD solution were prescribed for all CAPD patients while 7–9 exchanges during the night (8–10 h) with a single dwell volume of 2–2.5 l of 1.36% glucose PD solution and a single exchange during the day time (7–8 h) with a volume of 2 l of a 1.36% glucose PD solution were prescribed for all APD patients; APD patients were allowed to have a dry period (7–10 h) during the day. The median durations of PD at the time of the second and third PETs were 3.7 (3.0–4.9) months and 16.4 (14.9–17.8) months, respectively.

The peritoneal transport characteristics obtained during the first, second and third PETs in all patients are summarized in Table 1. The ultrafiltration (UF) was stable and the peritoneal membrane transport showed a progressive not significant increase over time.

Peritoneal transport characteristics obtained during the first, second and third PETs in the two groups of patients (CAPD and APD) are shown in Table 2. The only difference between the two groups was the age at the beginning of CAPD or APD (66.8 ± 10.8 versus 56.2 ± 10.0 years, respectively, P = 0.008).

After the first PET and before the second PET, four patients were shifted to haemodialysis because of catheter malfunction (two patients) or major surgical abdominal procedure (two patients); one patient was transferred to another centre. After the second PET and before the third PET, three patients died, four patients were shifted to haemodialysis because of severe fluid overload and two patients were transferred to another centre.
Between the first and second PETs, the UF did not change, while the peritoneal membrane transport increased in CAPD patients but remained stable or decreased in APD patients.

Between the second and third PETs, the UF was stable and the peritoneal membrane transport slightly increased both in CAPD and APD patients.

Patients were then evaluated with a more sophisticated analysis according to the number of PETs performed and independently analysed as different cohorts, as described above.

In patients with at least two PETs, the only difference at the start of CAPD or APD was the age (68.3 ± 8.7 versus 56.3 ± 10.5 years, respectively, $P = 0.002$). This was the only difference also for the patients who had undergone at least three PETs (66.8 ± 8.4 years for CAPD versus 53.5 ± 8.0 years for APD, $P = 0.002$).

Figure 1A shows the changes over time of peritoneal membrane transport in the patients with at least three PETs. The UF did not change over time (data not shown) but the other parameters of peritoneal membrane transport indicated an early increase in peritoneal transport only in CAPD patients whereas the peritoneal transport was steady or decreased in APD patients in the early period. Then, the peritoneal membrane transport was steady or slightly increased both in CAPD and in APD patients remaining higher in CAPD patients than in APD patients.

Figure 1B shows the changes of peritoneal membrane transport between the first and second PETs. The data confirmed the early increase of peritoneal membrane transport only in CAPD patients.

Figure 1C shows the changes of peritoneal membrane transport between the second and third PETs. A slight increase of peritoneal membrane transport was observed both in CAPD and APD patients but with a significant difference over time between the peritoneal membrane transport of CAPD and APD patients (only D/D0 decreased significantly in APD patients and tended to values similar to those of CAPD patients).

The urine output was 1550 (1000–2000) ml, 750 (450–1400) ml and 550 (225–1600) ml at the first, second and third PETs, respectively. The urine output decreased significantly ($P < 0.001$), and the reduction was similar in CAPD and APD patients ($P = 0.855$).

The GFR was 4.3 (3.1–5.5) ml/min/1.73 m², 2.4 (1.3–3.8) ml/min/1.73 m² and 1.7 (0.6–3.9) ml/min/1.73 m² at the first, second and third PETs, respectively. The GFR decreased significantly ($P < 0.001$), and the reduction was similar in CAPD and APD patients ($P = 0.118$).

During the study, there were four cases of peritonitis, three in CAPD patients (two in the period between the first and second PETs and one in the period between the second and third PETs) and one in APD patients (in the period between the first and second PETs). The MANOVA did not show any influence of peritonitis on peritoneal membrane transport.

**Discussion**

The results of this small, single-centre study suggest that performing the PET before and after the start of PD could provide relevant information about the characteristics of small solute peritoneal membrane transport and could be useful to evaluate the influence of PD modality on the changes in peritoneal membrane transport.

In this study, the small solute transport of peritoneal membrane, assessed before and after the start of PD, changed differently in patients on CAPD or APD. Before the start of PD, the two groups of patients had similar characteristics except that patients on CAPD were older. After the start of PD, a marked increase in peritoneal membrane transport was observed in patients on CAPD during the first months of treatment, and this increase persisted 16 months after the beginning of PD. In contrast, the small solute peritoneal membrane transport remained unchanged in patients on APD during the first months of treatment and had a slight increase 16 months after the start of PD. The UF remained unchanged in both PD modalities probably because the follow-up was not sufficiently long. To our knowledge, this is the first study that evaluated the changes in the small solute transport of peritoneal membrane before the start of PD and after a short and a relatively long period from the start of PD.

The characteristics of peritoneal membrane transport before the start of PD were assessed in the past [20]; however, they were compared to those of patients on chronic PD and were not revaluated after the start of PD. Other studies, conducted in CAPD patients, have demonstrated a rise in small solute transport of peritoneal membrane when it was assessed with the PET during the first month of PD or after the first month of PD [13,14]; on the basis of these studies, it was recommended to perform the PET after the first month of PD, in order to avoid classifying the same patient

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**Table 2. Peritoneal membrane characteristics in CAPD and APD patients**

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<tr>
<th></th>
<th>First PET</th>
<th>Second PET</th>
<th>Third PET</th>
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<tbody>
<tr>
<td></td>
<td>CAPD</td>
<td>APD</td>
<td>CAPD</td>
</tr>
<tr>
<td>UF (ml)</td>
<td>770 ± 308</td>
<td>742 ± 233</td>
<td>793 ± 208</td>
</tr>
<tr>
<td>D/D0</td>
<td>0.25 ± 0.07</td>
<td>0.28 ± 0.06</td>
<td>0.21 ± 0.05</td>
</tr>
<tr>
<td>D/P creati</td>
<td>0.66 ± 0.12</td>
<td>0.64 ± 0.12</td>
<td>0.73 ± 0.07</td>
</tr>
<tr>
<td>D/PA 60′</td>
<td>0.90 ± 0.03</td>
<td>0.89 ± 0.03</td>
<td>0.90 ± 0.02</td>
</tr>
<tr>
<td>Patients no.</td>
<td>22</td>
<td>12</td>
<td>18</td>
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</table>

PET, peritoneal equilibration test; CAPD, continuous ambulatory peritoneal dialysis; APD, automated peritoneal dialysis; UF, ultrafiltration.
in different classes of transporters before and after the first month of PD. The results of these studies indicate that PD causes an early increase in peritoneal membrane transport. The mechanisms underlying these observed early changes in membrane transport remain uncertain. The contact between the peritoneal membrane and the dialysis fluid could result in an increased local production of cytokines and vasodilatation [21]. A peritoneal membrane with relatively increased blood flow or an increased number of perfused capillaries in contact with dialysis fluid could result in a higher small solute rate [22].

The results of our study suggest that the early changes in peritoneal membrane transport could be influenced by PD modality at the start of PD. The data of this study do not allow us to explain the reasons of this finding; however, some hypotheses could be formulated. The first hypothesis is that, in dry-day APD patients, the period of time (7–10 h) during which the peritoneal cavity is not filled with dialysis fluid could allow the temporary restoration of the normal haemodynamics of the peritoneal microcirculation. This would lead to the reduction of the peritoneal capillaries' vasodilatation, which is probably the cause of the early increase in the small solute transport of peritoneal membrane. Another hypothesis (that could be complementary to the first) is that, in APD, the time of contact between the peritoneal membrane and the dialysis fluid could be shorter because of the numerous dwells, so that there are more periods of time (the infusion and the draining) during which only limited areas of peritoneal membrane are in contact with the dialysis fluid. The anatomical area of membrane in contact with dialysis fluids can influence the small solute transport of peritoneal membrane as evidenced by the clinical data linking transport rate to body size and habitus [8,11,23], and the increased fill volume is associated with greater contact area on computerized tomography scan and higher solute transport [24]. The early changes in the peritoneal membrane in response to intraperitoneal fluid (and increases in hydrostatic intraperitoneal pressure) could be quite different for CAPD and APD. During the first few dialysis sessions in CAPD, there is a considerable increase in interstitial volume [25]. These changes may be less pronounced in APD patients. Because of this, APD patients may show higher interstitial transport resistance and lower peritoneal membrane transport than CAPD patients. These mechanisms could counterbalance the greater exposure to glucose that occurs in APD.

The study of the possible influence of PD modality on small solute transport would be of great interest. In fact, since an increased small solute transport of peritoneal membrane has been associated with higher mortality and

Fig. 1. Small solute peritoneal membrane transport in CAPD and APD patients during the follow-up (A), between the first and second PET (B) and between the second and third PET (C).
technique failure [11,12], it could be inferred that the use of a PD modality that is not associated with an increase of small solute transport could be beneficial to patients on PD.

This study suggests that performing the PET only some months after the start of PD (for example 4 months after the start of PD, as the second PET of this study) could bring to different conclusions. Observing Figure 1C, one would conclude that the two groups of patients on CAPD and APD had different characteristics of small solute transport since the ‘beginning’ of PD (as shown by the PET performed after 4 months of PD) and that the small solute transport remained unchanged in CAPD patients and increased in APD after about 1 year of PD. In this case, the conclusions would be the opposite of the conclusions drawn performing the first PET at the actual start of PD.

This study is characterized by some limitations such as the small sample size and the lack of randomization to PD modality, so the results should be confirmed by a randomized study with a greater sample size. Even if it is very difficult to randomize patients to PD modality not considering the patients’ and their families’ preferences, the results of a randomized study would be of great interest because they would affect a core issue in PD: is there a starting PD modality of choice?

On the basis of the results of this study, we estimated the sample size to conduct a randomized controlled study: considering a clinically relevant difference of 1 SD in the parameters of peritoneal membrane transport (the same used for the classification of PD patients in different classes of transporters), a 50% of patients lost in 1 year of follow-up and assuming a type I error of 5% to obtain a 90% power, a sample size of 120 patients (60 in each group) would be required [23]. So, a randomized study could be possible only in the case of a multicentre study.

Another limitation of this study is the older age of the patients starting CAPD in comparison with patients starting APD. Some studies have reported that age, male gender, race and other factors are associated with higher peritoneal solute transport; however, less than 20% variance in solute transport can be explained by all these factors [26]. Moreover, in this study, the age does not seem to influence the small solute transport of peritoneal membrane at the beginning of PD.

In conclusion, this study, that evaluated for the first time the small solute transport of peritoneal membrane before and after the start of PD, points out that performing the PET before and after the start of PD could provide relevant information about the characteristics of small solute peritoneal membrane transport and suggests the possibility that the PD modality could have an early influence on the small solute transport of peritoneal membrane.

Conflict of interest statement. None declared.

References

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